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Food Intake, Fuel Homeostasis, and the Autonomic Nervous System.

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The mobilization, storage and utilization of the different energy substrates is regulated by sensitive and very specific hormonal and neural mechanisms. Increased parasympathetic activity leads to storage of glucose and free fatty acids (FFA) while activation of the sympathetic branch of the autonomic nervous system (ANS) results in the mobilization of FFA and glucose from storage tissues. The latter is accomplished by both neuronal norepinephrine (NE) in the periphery and hormonal epinephrine (E) from the adrenal medulla.

The relation between autonomic activity and substrate availability might be bidirectional: an increased availability of energy substrates could activate the parasympathetic branch of the ANS, while a decreased availability of glucose and/or FFA may lead to increased sympathetic outflow. One set of experiments investigated the metabolic and hormonal responses that occur during food intake or intravenous or intragastric administration of glucose (Strubbe, 1992). Food intake was accompanied by the early insulin response (EIR), an increase in plasma insulin that occurs immediately after the onset of a meal. The EIR could be suppressed by prior administration of atropine or subdiaphragmatic vagotomy. Administration of atropine also attenuated and delayed the insulin response to intravenous or intragastric glucose load indicating that the parasympathetic nervous system is also involved in the dynamics of insulin secretion during hyperglycemia.

A second set of experiments was conducted to examine the metabolic and hormonal responses to a reduction in the availability of energy substrates (Scheurink & Ritter, 1993; Van Dijk *et al.*, 1995). Hypoglycemic doses of insulin or drugs that block glucose (2-deoxy-D-glucose, 2DG) or FFA (mercaptoacetate, MA) utilization were i.v. administered and catecholamine responses were measured. Glucoprivation was accompanied by a robust stimulation of adrenal E secretion combined with a small NE outflow. Lipoprivation stimulated only the neuronal branch of the sympathetic nervous system without any effect on adrenal E release. The finding that decreased glucose availability leads to adrenomedullary secretion of E is compatible with the fact that circulating E is an important mediator of hepatic glucose production in rats. Likewise, the selective increase in neuronal outflow of NE after MA administration can be considered a metabolically appropriate response to blockade of FFA oxidation since neuronal NE serves as the physiological mediator of lipolysis in white adipose tissue. These data indicate that distinct metabolic signals are capable of exerting a selective and functional control of sympathoadrenal outflow.

The hypothalamus is the likely source of control (Scheurink & Steffens, 1990). A possible mechanism is serotonin (5-HT) as it is able to affect E outflow without affecting NE release. When administered to sleeping rats, fenfluramine is associated with a rise in E and has no effect on NE. There is also a corresponding increase in circulating glucose while FFA levels remain unchanged. These effects can be blocked by 5-HT-1a receptor blockade. In preliminary studies, i.v. administration of 2DG increased hypothalamic 5-HT in medial hypothalamus measured by microdialysis and increased circulating levels of E. MA administration did not affect either medial hypothalamic 5-HT levels or plasma E.

Taken together, the data demonstrate that metabolic needs are regulated via changes in the functioning of the different branches of the autonomic nervous system. In turn, metabolic states can also profoundly affect the functioning of the autonomic regulatory mechanisms. The hypothalamus may function as a center in the brain coordinating autonomic outflow and energy balance.

Scheurink, A. & Ritter, S. (1993) Sympathoadrenal responses to glucoprivation and lipoprivation in rats. *Physiology and Behavior*, *53*, 995–1000.

Scheurink, A. J. W. & Steffens, A. B. (1990) Central and peripheral control of sympathoadrenal activity and energy metabolism in rats. *Physiology and Behavior*, *48*, 909–20.

Strubbe, J. H. (1992) Parasympathetic involvement in rapid meal-associated conditioned insulin secretion in the rat. *American Journal of Physiology*, *263*, R615–18.

Van Dijk, G., Scheurink, A. J. W., Ritter, S., & Steffens A. B. (1995) Glucose homeostasis and sympathoadrenal activity after lipoprivation in rats. *Physiology and Behavior*, *57*, 759–64.

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